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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/581,967	06/19/2000	Bertil Abrahamsson	1103326-0624	6706

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EXAMINER	
YOUNG, MICAH PAUL	
ART UNIT	**PAPER NUMBER**
1618	

DATE MAILED: 01/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/581,967	ABRAHAMSSON ET AL.	
	Examiner	Art Unit	
	Micah-Paul Young	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29 and 33-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29 and 33-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment of Papers Received: Amendment/Response dated 10/14/05.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claim 29, and 36-40 is rejected under 35 U.S.C. 102(b) as being anticipated by Brieaddy et al (USPN 5,723,458 hereafter '458). The claim is drawn to a pharmaceutical formulation comprising a core with a coating. The core comprises core materials and an IBAT inhibitor. The formulation releases in the colon.

3. The '458 patent discloses formulation comprising a core with core materials and a coating. The active agent of the formulation is an IBAT inhibitor, specifically 1,4-benzothiazepin compounds (examples). The formulation is formed into tablets and coated with enteric polymers (col. 9, lin. 60- col., 10, lin. 20). The uncoated tablet acts as a core, and comprises tableting materials such as binders, lubricants and diluents (*ibid.*), including resins such as povidone (examples). Due to the nature of enteric coatings, the active agent is released in the lower intestine. These disclosures render the claims anticipated.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 33-35 and 41-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Brieaddy et al (USPN 5,723,458 hereafter '458), Hirakawa et al (USPN 5,614,220 hereafter '220) and Lee et al (USPN 5,994,391 hereafter '391). The clams are drawn to a pharmaceutical formulation comprising a core, core material and a coating. The claims are further drawn to a method of treating hypercholesterolemia and side effects associated with an IBAT treatment.

7. As discussed above the '458 discloses a coated benzotheipine tablet. The tablet due to its enteric coating will release in the lower intestine, yet does not disclose specifically the ileum or a treatment of hypercholesterolemia.

8. Regarding the release of the formulation, the targeted release of an active agent is well within the level of skill of an ordinary artisan. This level of skill can be seen in the '220 patent which discloses the targeted release of active agents including antilipedemic, and hypoglycemic drugs (col. 4, lin. 24-37). The formulation comprises a core and an enteric coating (col. 2, lin. 38-45). The formulation is coated to release anywhere in the intestinal track beyond the stomach

(abstract). The core is protected by the enteric coating and does not release the contents of the core for up to 3±1 hours, the time needed to travel through the small intestine (col. 3, lin. 54-col. 4, lin. 23). The active agent is designed for release in the lower colon (*ibid.*). The core is formed with binders, lubricants and other necessary polymers and excipients, including water-soluble polymers (col. 6, lin. 57-68- col. 7, lin. 15). A skilled artisan would be motivated to formulate the coated tablets '458 with the process of '220 in order to provide targeted release of the IBAT inhibitor. Since the both formulations comprise enteric coatings, and the cores comprise water-soluble polymers and well-known excipients, this would be well within the level of skill in the art to combine the teachings.

9. Regarding the hypercholesterolemia treating properties of the IBAT inhibitors, this property is inherent to the formulation and would be apparent to one of ordinary skill in the art as seen in the '391 reference. The '391 reference discloses various IBAT inhibitors including 1,4-benzothiazepine (abstract, examples) treating hypercholesterolemia. A skilled artisan would be able to use the formulation of '220 to treat hypercholesterolemia since the formulation would inherently have this property.

10. Regarding the bile acid binder and the treatment of diarrhea, applicant recites that the bile acid binder is a resin, which reads broadly on any polymer coupled with the IBAT inhibitor. No further limitations are given for the resin. It is the position of the examiner that any polymer in mixture with the IBAT inhibitor and released properly would act as a bile acid binder. The combination of reference provides a formulation with an IBAT inhibitor and a water-soluble polymer, binder and/or lubricant in the core. The core is designed to dissolve in the large

intestine and release the active agent in the lower intestine (colon). These disclosures render the claimed invention obvious barring evidence to the contrary.

11. With these things in mind, it would have been obvious to combine the teachings of the prior art. A skilled artisan would have been motivated to formulate the IBAT inhibitor coated tablets of '458 as shown in '220 in order to release the IBAT inhibitor in the lower intestine for optimum treatment. Further the artisan would have been motivated to combine these teachings since the formulation both comprise similar structures, namely active agent cores mixed with core materials, protected by an enteric coating. A skilled artisan would have followed the motivation of '391 to use this formulation to treat hypercholesterolemia. It would have been obvious to combine these teachings, suggestions and motivations with an expected result of a coated tablet capable of treating hypercholesterolemia.

Response to Arguments

12. Applicant's arguments filed 10/14/05 have been fully considered but they are not persuasive. Applicant argues that:

a. The '458 reference art does not teach or suggest an oral formulation comprising an IBAT inhibitor compound and a bile acid binder.

b. Since the '458 patent does not teach the combination of a bile acid binder and an IBAT inhibitor, the combination of reference does not obviate the instant invention.

13. Regarding argument a., it is the position of the Examiner that given the broadest reasonable interpretation of the claims, the '458 reference discloses an oral formulation comprising an IBAT inhibitor compound along with a compound capable of binding bile acids. The reference teaches a composition comprising specifically 1,4-benzothiazepin and binding

agents. These binding agents include povidone, which is a resin. Applicant defines the bile acid binders as resins, which are polymeric compounds used for binding. Povidone, as used by the '458 patent, is a well-known binding agent. Although the property is not recognized in the art, applicant clearly defines the bile acid binders a resin. Burden is shifted to applicant to provide evidence that povidone **cannot** bind **any** bile acids. Further regarding the structure, applicant argues that the bile acid binder is coated and suggests that only the bile acid binder is coated, while the remainder of the formulation remains uncoated. Applicant argues that only the bile acid binder is coated in the core unlike the entire dosage from of the '458. However, the uncoated tablets of the '458 comprising the binders, excipients and IBAT inhibitor act as the core of the formulation. By the nature of the coating the release would be targeted for the intestinal track. It is well within the level of skill in the art to manipulate the release location. For these reasons the claims remain anticipated by the '458 patent.

14. Regarding argument b., as discussed above the '458 patent teaches an oral IBAT inhibitor, yet is silent to the specific release locations. The '220 patent teaches the targeted release of active agents, and establishes the level of skill in the art regarding this technology. The supporting references show the level regarding the targeted release of various active agents. The '391 patent teaches the level of skill in the art regarding treating hypercholesterolemia with composition of the combination. It would have been obvious to combine the teachings and suggestions in the art to treat hypercholesterolemia and for targeted release in the intestinal tract. For these reasons the claims remain obviated by the art.

Conclusion

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Micah-Paul Young whose telephone number is 571-272-0608. The examiner can normally be reached on M-F 7:00-4:30 every other Monday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Micah-Paul Young
Examiner
Art Unit 1618

MP Young

MICHAEL HARTLEY
PRIMARY EXAMINER